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EXAMINER	
SISSON, BRADLEY L	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	09/445,205	GALZI ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-52* is/are rejected.

7)☒ Claim(s) *37-38* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Objections

1. Claims 37 and 38 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 37 teaches the use of a non-labeled ligand. Such method step is considered to broaden the scope of claim 36, from which it depends, as claim 36, line 33, states that the ligand is labeled. Claim 38, which depends from said claim 37, fails to overcome this issue and is similarly objected.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 36-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. As presently worded, claim 36, second indent, states that the cell or cell fragments contain "a DNA sequence comprising a gene expressing a fluorescent protein fused with a gene for the target protein." It is unclear if applicant intended to have a protein fused to a gene (DNA) or whether there are two genes that are linked such that they give rise to a fused protein. Claims 37-46, which depend from said claim 36, fail to overcome this issue and are similarly rejected.

5. Claim 38 is indefinite with respect to what the abbreviation "EGFP" stands for. Applicant is urged to amend the claim such that the full name occurs prior to the first usage of the abbreviation in a given series of dependent claims.

6. Claim 50 is indefinite with respect to what the abbreviations "EYFP," "EGFP," AND "ECFP" stand for. Applicant is urged to amend the claim such that the full name occurs prior to the first usage of the abbreviation in a given series of dependent claims.

7. Claim 37 is indefinite with respect to how a "decrease in the amplitude of the donor's emission, and/or emission signal characteristic of the acceptor's emission is detected" when this "decrease" is to be measured "before" other specified steps.

8. Claims 36-48 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: The performance of a comparison or calibration step such that any signal detected and measured can in tern be reasonably quantified. As presently worded, one is to "optionally [measure] the fluorescence energy transfer when quantifying the non-covalent interactions." However, there is no relationship established between the quantity of any labeled added and any control. In fact, there need not be any reference point. Applicant is urged to consider amending the claims such that some frame of reference is utilized when performing the quantitative aspect of the method.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision of *Vas-Cath Inc. v. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

> This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

Attention is also directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

10. Claims 36-46 and 52 are drawn to a "[p]rocess for detecting and/or quantifying non-covalent interactions between a target protein and one of its ligands." Claim 47 is drawn to a "[p]rocess for detecting and/or quantifying non-covalent interactions between a target protein consisting of a receptor coupled to G proteins and a G protein, in order to identify molecules which are biologically active with respect to the receptor, and which are capable of forming a reversible non-covalent interaction with said receptor." And claims 49-51 are drawn to "kit or equipment for detecting and quantifying non-covalent interactions between a target protein

labeled with a first fluorescent protein and one of its ligands labeled with a fluorescent substance corresponding to a second fluorescent protein." A review of the disclosure finds general teachings as to how starting materials may be produced and directs the public to publications as to prior art methods that may be useful in practicing the claimed methods.

11. While applicant states at page 2 of the disclosure that "[t]he invention relates, in particular, firstly to the preparation of target protein, especially receptors, made fluorescent by fusion with a fluorescent protein, secondly to their labeled ligands," the claims are not drawn to process for the production of the materials to be used in the later-disclosed methods. General and at times, motivating statements for the identification of starting materials, and indeed, the materials themselves, as claimed in the kits, does not reasonably suggest that applicant was in possession of the claimed method or the kit/equipment claimed instantly.

12. The declaration under Rule 132, filed on 09 September 2002, has been fully considered and has not been found persuasive. It is noted that declarant is the first-named inventor of the instant application and as such is recognized as having a vested interest in the proceedings before the Office and does not constitute the opinion of a disinterested third party.

13. Page 2 of the declaration states:

> Variants of the fluorescent protein include all mutations in the DNA sequence that lead to a protein with a primary amino acid sequence identical to, or different from, the wild type sequence...Many mutations done in the DNA sequence encoding GFP lead to fluorescent proteins with identical, different or no fluorescent properties.

At page 3 declarant states:

> Fragments of the fluorescent protein include deletions or additions of amino acids at both N-terminal and C-terminal extremities....
>
> Variants and fragments can be obtained by random mutagenesis, by site-directed mutagenesis, or by using restriction endonucleases acting on the DNA.

In order to practice the claimed methods, and to assemble the claimed kits, one must have the requisite starting materials and components. Declarant does not direct attention to where the specification discloses the innumerable compounds and compositions claimed, or required for the kit. While an application need not set forth each and every possibly embodiment, the specification must set froth a reasonable number of embodiments in such full, clear, and concise language so as to reasonably suggest that applicant was in possession of the invention at the time of filing. In support of this position, attention is directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.
>
> ***
>
> We are of the opinion that a genus containing such a large number of species cannot properly be identified by the mere recitation or reduction to practice of four or five of them. As was pointed out by the examiner, four species might be held to support a genus, if such genus is disclosed in clear language; but where those species must be relied on not only to illustrate the genus but to define what it is, the situation is otherwise.

It would appear that applicant is attempting to rely upon obviousness for the skilled artisan to produce the requisite starting materials, as well as the components of the kit/equipment. Obviousness, however, is not available in overcoming the requirements of written description. In support of this position, attention is directed to the decision in *University of California v. Eli*

Lilly and Co. (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

While declarant states at page 5 as to how the method is to be practiced, such does not overcome the deficit in starting materials and reaction conditions under which the claimed invention is to be practiced. Additionally, the statements do not reasonably suggest that applicant was in possession of the claimed kit and equipment components. Therefore, and in the absence of convincing evidence to the contrary, the rejection is maintained.

14. Claims 36-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135, bridging to 1136:

> To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, *e.g.*, *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining

> whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

15. As set forth above, the specification does not reasonably suggest that applicant was in possession of the invention. Accordingly, one cannot enable the use of that which they do not yet possess.

16. The claimed methods relate to matters of physiology and chemistry. Such areas of art are recognized as being unpredictable and deserving of greater levels of disclosure so as to enable the claimed invention. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

> In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

A review of the disclosure fails to find an example where specific starting materials, and reaction conditions are set forth whereby non-covalent interactions between a target protein and one of its ligands was detected and quantified. A review of the disclosure finds 11 examples:

1. Example 1, pages 45-46, “”DNA CONSTRUCTS COMPRISING A FUSION BETWEEN EGFP AND THE AMINO-TERMINAL END OF THE NK2R RECEPTOR OF TACHYKININS;”

2. Example 2, pages 46-47, "CONSTRUCTION OF DNA COMPRISING THE FUSION OF GFP INTO THE INTRACELLULAR LOOPS 11 AND 13 OF THE TACHYKININ NK2R RECEPTOR;"

3. Example 3, pages 47-50, "EXPRESSION OF RECOMBINANT PROTEINS AND FUNCTIONAL CHARACTERIZATION;"

4. Example 4, pages 50-51, "PREPARATION OF FLUORESCENT LIGANDS;"

5. Example 5, pages 51-54, "DETECTION OF THE INTERACTION BETWEEN THE FLUORESCENT NK2R RECEPTOR AND ITS FLUORESCENT LIGANDS;"

6. Example 6, page 54, "CLONING OF THE NK2R-RF1 CDNA INTO THE VECTOR PPIC9 AND EXPRESSION IN THE YEAST *PICHIA PASTORIS*;"

7. Example 7, pages 55-56, "CONSTRUCTION OF DNA CODING FOR THE MUSCARINIC RECEPTOR OF ACETYLCHOLINE FUSED WITH EGFP AND EXPRESSION IN MAMMALIAN CELLS;"

8. Example 8, pages 56-57, "DNA CONSTRUCTS CODING FOR FLUORESCENT NICOTINIC RECEPTORS;"

9. Example 9, pages 57-58, "DNA CONSTRUCT CODING FOR A FLUORESCENT CHEMOKINE RECEPTOR;"

10. Example 10, pages 58-59, "DNA CONSTRUCT CODING FOR THE FLUORESCENT HUMAN CHEMOKINE RANTES;" AND

11. Example 11, pages 59-61, "IDENTIFICATION OF NOVEL LIGANDS FOR ORPHAN RECEPTORS."

12. Of the 11 examples, Example 11 would appear to be the most relevant to the claimed invention. A review of the example, however, finds that the method more closely describes cloning procedure and that no novel ligand has been identified. Accordingly, the specification has not been found to set forth the reaction conditions and starting materials that are required to practice the claimed invention. As shown above, such information is considered to be critical in practicing the invention and to not disclose such would cause skilled artisans to resort to trial-and-error experimentation with little if any reasonable expectation of success. While 35 USC 112, first paragraph, allows for some experimentation, the absence of critical teachings in instant disclosure would cause the pubic to resort to a level of experimentation deemed undue.

13. For the above reasons, and in the absence of convincing evidence to the contrary, claims 36-47 and 52 are rejected as not being enabling. Similarly, the specification has not been found to enable use of the kits and equipment of claims 49-51.

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

15. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is 703-308-3978. The examiner can normally be reached on Monday through Thursday from 6:30 AM to 5 PM.

17. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

18. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
August 10, 2003